REMARKS/ARGUMENTS

I. Status of claims

Claims 1, 14 and 15 are amended.

Claims 5-9 were withdrawn previously as they referred to non-elected species. Applicants reserve the right to rejoin these claims if the elected species are found to be allowable.

Claims 11-13 are canceled.

Claims 1-4, 10, 14-57 are being examined.

II. Benefit of Priority Extends to the Filing Date of the Provisional Application.

The examiner alleges that the provisional application does not comply with the requirements of 35 U.S.C. §112 first paragraph because the examiner believes that the provisional application "does not provide a detail support for the broadly claimed scope drawn to any human cell line except K562". (page 2, Office Action). Applicant is unsure as to what is meant by "detail support". The provisional application as filed provides adequate support for the pending claims. K562 cell line was an exemplary embodiment. Case law is inapposite to the flawed requirements imposed by the Office Action. See e.g., "The earlier application need not describe the claimed subject matter in precisely the same terms as found in the claims at issue." *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1331 (Fed. Cir. 2008). The provisional application as filed describes "treating patients with cancer", "EBV-associated malignancies", and "cell vaccines for treating EBV (+) tumors" under the Abstract as well as the Detailed Description sections of the application.

Therefore, the provisional application adequately supports the pending claims under 35 U.S.C. §112 first paragraph requirements. Applicants request the examiner to accord benefit of priority of the filing date of the provisional application 60/411,990, filed September 19, 2002.

III. Claims 1-4, 10, and 14-15 satisfy 35 U.S.C. §112 written description and enablement requirement.

The Examiner on page 3 of the Office Action rejected claims 1, 4, 10, and 14-15 for lack of written description requirement because the Examiner believes that it would require undue experimentation to practice the claims.

The Examiner acknowledges:

> Based on specification, Applicants do not show reduction to the practice for any other human cell lines [sic] except K562 for deficiency in MHC-1 and MHCII, but expressing an EBV antigen and an immunomodulator.

Page 4, Office Action.

Even though an actual reduction to practice is not required to demonstrate written description or enablement requirement, applicants have demonstrated an embodiment that adequately enables the full scope of the claims. See e.g., Cooper v. Goldfarb, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998) (A specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose.).

However, the Examiner, without support concludes:

> Because the claims encompass a genus of human cell lines, an sufficient [sic] evidence needs to be provided for a reduction of practice prior to the current application was originally filed and at least a representative number of species for such claimed human cell lines that had been isolated by actual reduction to practice.

Page 4, Office Action.

The examiner has not provided any specific evidence to show that the claimed compositions could not have been made by a person of ordinary skill in the art, based on the guidance and the available knowledge in the art. Mere fact that the compositions relate to human cell lines do not automatically render a heightened scrutiny under the section 112 test. According to *In re Bowen*, 492 F.2d 859, 862-63, 181 USPQ 48, 51 (CCPA 1974), the minimal requirement is for the examiner to give reasons for the uncertainty of the enablement. MPEP 2164.04.

The examiner has not shown that administering a sufficient amount of a human cell line that is deficient in major histocompatibility class I (MHC-I) antigens and major histocompatibility class II (MHC-II) antigens and which has been modified to express a gene encoding an immunomodulator and a gene encoding an antigen of Epstein-Barr virus (EBV) will not induce or stimulate an immune response to an EBV-associated cancer as in pending claims 16-57.

The examiner has failed to establish a prima facie case of lack of enablement because the examiner has not shown why a skilled artisan would not be able to obtain a human cell line, that lacks major histocompatibility class I (MHC-I) antigens and major histocompatibility class II (MHC-II) antigens and which has been modified to express (i) a gene encoding an immunomodulator and (ii) a gene encoding an antigen of Epstein-Barr virus (EBV).

The instant application, in some embodiments, provides compositions and methods relating to human cell line that lacks major histocompatibility class I (MHC-I) antigens and major histocompatibility class II (MHC-II) antigens and which have been modified to express an immunomodulator and an antigen of Epstein-Barr virus (EBV). Also provided by the present disclosure are methods of inducing or stimulating an immune response in a human to an EBV-associated cancer by administering one of the aforementioned compositions in an amount sufficient to induce or stimulate an immune response to the antigen of EBV expressed by the human cell line, whereupon an immune response to the EBV-associated cancer is induced. Thus, use of a bystander line, e.g., K562 obviates the need for *in vitro* passaging or modification, such as by transduction, of each patient's tumor cells, thereby guaranteeing a constant amount of cytokine production without any intra- or inter-patient variability, while utilizing the patient-specific antigenic repertoire.

The Examiner did not provide any evidence to show that generating a human cell line lacking MHC class I and class II antigens is not possible to practice the invention. To the contrary, the specification provides an exemplary cell line (K562) and on paragraph [0018], the application describes methods to generate human cell lines that are deficient in expressing MHC class I and II antigens on cell surface. The specification also mentions SK-MEL-33 as a suitable cell line (paragraph [0017] of the specification). In addition, the specification describes interfering with the expression and/or transport of α-chain of MHC class I antigens and α-β chains of MHC class II antigens. The specification also provides examples to generate suitable cell lines by providing dominant negative forms of the respective antigens and by transfection, retroviral infection or homologous recombination to achieve expression of modified MHC or β_2 microglobulin genes or inactivation of genes.

Nevertheless, to expedite prosecution, claims 1, 4, 10, and 14-15 are amended to include K562 as a suitable cell line. Applicants reserve the right to pursue composition and method claims involving cell lines other than K562 in continuing applications.

The specification provides adequate disclosure and guidance to enable a skilled artisan to practice the pending claims. Applicants request the Examiner to withdraw the §112 rejections for claims 16-57.

Applicants thank the examiner for withdrawal of prior art and other section 112 rejections.

No other fees are due. However, please charge any fees that might be due in connection with this submission to our Deposit Account No. 12-0913 with respect to our matter number 43369-103949.

Respectfully submitted,

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